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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/989,554	11/20/2001	David Carl Burdick	20257.US1/110716	2152

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EXAMINER	
QAZI, SABIHA NAIM	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 10/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/989,554	BURDICK ET AL.	
	Examiner	Art Unit	
	Sabiha Qazi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *19 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *9-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *9-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

OFFICE ACTION

Due to incomplete reference of Mishkel et al. listed in 892-form, Mr. Stephen Brown called to re-start the clock and requested to send a complete copy of the reference. (See telephonic interview). Acknowledgement is made of the response filed in paper no. 6, dated 5/19/03. Claims 9-14 are pending. No claim is allowed. The arguments were fully considered and were found persuasive in part. Rejection under 112 (2) is withdrawn because claim is amended.

The Examiner disagrees with the arguments because Higgins III US '068 does teach the presently claimed invention. It teaches the use of unsaturated fatty acid for the production of sterol ester. The unsaturated fatty acid includes linolenic acid and docosohexanoic acid, see US '068 in col. 2, lines 6 to 15.

See lines16 to 26 in col. 2 of US '236 for the same disclosure. Therefore, the Examiner disagree that CIP '236 does not teach the invention. Examiner agrees that examples and structures were not drawn in parent application however, the present invention was taught and considered obvious at the time of the invention.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill might reasonably infer from the teachings. *In re opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA 1976)

A reference is not limited to working examples. *In re Fracalossi* 215 USPQ 569 (CCPA 1982). Accordingly, the burden of proof is upon applicants to show that instantly claimed subject matter is different and unobvious over those taught by prior art. See *In re Brown*, 173 USPQ 685, 688; *In re Best*, 195 USPQ 430 and *In re Marosi*, 218 USPQ 289, 293.

Claim Rejections - 35 USC § 112

Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The first paragraph of 35 U.S.C. 112 states, "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...".

The courts have interpreted this to mean that the specification must enable one skilled in the art to make and use the invention without undue experimentation.

The courts have further interpreted undue experimentation as requiring "ingenuity beyond that to be expected of one of ordinary skill in the art" (Fields v. Conover, 170 USPQ 276 (CCPA 1971)) or requiring an extended period of experimentation in the absence of sufficient direction or guidance (In re Colianni, 195 USPQ 150 (CCPA 1977)).

Additionally, the courts have determined that "... where a statement is, on its face, contrary to generally accepted scientific principles", a rejection for failure to teach how to make and/or use is proper (In re Marzocchi, 169 USPQ 367 (CCPA 1971).

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described

in In re Colianni, 195 USPQ 150, 153 (CCPA 1977), have been clarified by the Board of Patent Appeals and Interferences in Ex parte Forman, 230 USPQ 546 (BPAI 1986), and are summarized in In re Wands (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed Cir. 1988).

Among the factors are the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the amount of direction or guidance present, the presence or absence of working examples, the breadth of the claims, and the quantity of experimentation needed. The instant disclosure fails to meet the enablement requirement for the following reasons:

Claim 14 is drawn to a process of lowering cholesterol and triglyceride levels in a mammal do not have complete support in the specification. There is no mention of ""process" anywhere in the disclosure for the process of lowering of cholesterol and triglyceride.

The state of the prior art and the predictability

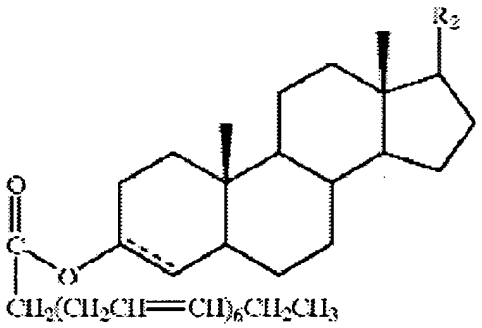
Prior art does teach lowering of cholesterol and triglyceride. In this art there is a lack of predictability. The process cannot be predicted

The amount of direction or guidance present

There are no working examples for the process as claimed in claim 14. Since no guidance is provided in the disclosure, one skilled in the art would not be able to practice the invention without undue experimentation. As cited above the requirement of 112 (1) that the invention should be described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

1. Claim(s) 9-14 is rejected under 35 U.S.C. 103 as being unpatentable over Higgins, III (US Patent 5,892,068) and Higashidate et al. (J. of

Chromatography, 515 (1990), 295-303). The references teach stero/stanol esters of poly unsaturated fatty acids and methyl esters of docosahexaenoic acid (DHA), which embrace instantly, claimed invention. See the entire documents especially lines 54-62 in col. 1; lines 6-15, col. 2 in US '068. See also claim 1 and examples for the method of preparation of sterol esters. This compound is specifically taught by US '068 (lines 14 in col. 2).



β-sitosterol docosahexaenoate; and
β-sitostanol docosahexaenoate

See abstract and first Para on page 295, Table 1 and last two paragraphs on page 302 in Higashidate reference.

Instant claims differ from the reference in claiming nutritional supplement of specific sterol esters from C18 to C22 having at least three double bonds whereas prior art US '068 teaches sterol esters with unsaturated fatty acids, example given contains at least three double bonds (DHA) which is the same as one of the instantly claimed sterol ester i.e. sterol with DHA, sitosterol docosahexaenoate and sitostanol docosahexaenoate.

Higashidate teaches DHA and EPA from fish oils and prevent diseases such as arteriosclerosis and myocardial infarction by lowering the concentration of lipids and cholesterol in blood. It discloses that fish oil is a rich source of such fatty acids.

It would have obvious to one skill in the art to prepare additional beneficial nutritional supplement using sterols with a pendent ester functionality which when hydrolyzed provides another cholesterol-lowering agent. Since Higgins teaches such sterol esters and Higashidate teaches that fish oil contains omega-3 fatty acids (a class of PUFA) which includes docosahexaenoic acid (DHA) and eicosahexaenoic acid (EPA), one would find ample motivation to prepare sterol esters with unsaturated fatty acids from active compounds present in fish oil (known to be used as nutritional supplement to lower the cholesterol and triglyceride levels) or using unsaturated fatty acids from any other source for use as nutritional supplement.

2. Claim(s) 9-14 are rejected under 35 U.S.C. 103 as being unpatentable over combined teachings of Mitchell (US 4,588,717) and Gregory J. Mishkel et al. (Bailliere's Clinical Haematology, Vol. 3, No. 3, July 1990, pp 625-649) and Kamarei et al. (US 4879,312). See the entire documents.

Mitchell (US Patent 4,588,717) teaches vitamin supplements containing phytosterol esters such as fatty acid esters of sterol, stigmasterol and

taxasterol, in various combinations, a composition of the phytosterols, such as sitosterol, stigmasterorl, taraxasterol etc. reacted with polyunsaturated fatty acids such as linoleic acid, (18-carbons, two double bonds), linolenic acid (18-carbons, 3-double bonds), arachidonic acid (20-carbons, two double bonds). Fatty acid may have about 18-20 in addition to two carbon atoms of terminal carboxyl and methyl groups (lines 2-15, col. 6) and at least two double bonds such as arachidonic acid, linoleic acid and linolenic acids are used to make phytosterol esters, (see lines 21-58, col. 3; lines 43-65, col. 5; equation 1 and lines 1-11 in col. 8). Furthermore, it teaches that the reaction between any given phytosterol and any given fatty acid is essentially the same, and is characterized in equation 1 using sitosterol and linoleic acid as an exemplary fatty acid.

Mishkel et al. teaches that fish oil containing omega-3 fatty acids lower the serum and cholesterol levels, and their beneficial effect on preventing and treating cardiovascular disease. See 1st Para on page 626, third paragraph on page 629, second Para on page 628. See also last three paragraphs on page 632, Figure 3 on page 630. Specific use of DHA and EPA as dietary supplement are disclosed in section "Angina" on page 634.

Kamarei et al. teach that a diet rich in omega-3-fatty acids has beneficial effects in humans, including a reduction in plasma cholesterol and triglyceride levels, improved fat tolerance, prolonged bleeding time reduce platelet counts

and decreased platelet adhesiveness. The omega-3-fatty acids are obtained mainly from dietary seafood. It teaches *n-3 Poly unsaturated fatty acids (PUFA) participation* and reasons why these materials may be involved in alleviating ischemic heart diseases. Furthermore, it also teaches that one of n-3 PUFA i.e. EPA and DHA reduces triglyceride and very low-density lipoprotein (VLDL) serum levels and reduces whole blood viscosity. (See lines 39-59, col. 2; lines 13-54, col. 3; Table 1 and 2 in col. 4).

Instant claims differ from the reference in claiming nutritional supplement of phytosterol ester with specific fatty acids i.e. containing atleast 3 double bonds from *C18 to C22* such as docosahexaenoic acid, where US '717 teaches phytosterol ester with fatty acids especially containing poly unsaturated fatty acid approximately *2-22 carbon atoms*. See examples 51-75 in col. 6, equation 2 in cols 15, 16, 17 and 18. Mishkel et al. teaches that polyunsaturated fatty acids from fish oil is used to preventing and treating cardiovascular disease. Furthermore, it teaches two major biologically active fish oil compounds, EPA and DHA. Kamarie teaches n-3 PUFA i.e. eicosapentaenoic acid (EPA) and DHA reduces triglyceride and very low-density lipoprotein (VLDL) serum levels and reduces whole blood viscosity. (See lines 39-59, col. 2; lines 13-54, col. 3 and Table 1 and 2 in col. 4).

It would have been obvious to one skilled in the art to prepare additional beneficial nutritional supplement using sterols with a pendent ester functionality which when hydrolyzed provides another cholesterol-lowering agent. Since Mishkel teaches that fish oil contains omega-3 fatty acids (a class of PUFA) which includes docosahexaenoic acid (DHA) and eicosahexaenoic acid

(EPA), see especially last Para on page 625 of Mishkel reference). There has been ample motivation provided by the prior art to prepare the instant invent

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi whose telephone number is 703-305-3910. The examiner can normally be reached on every business day..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

October 30, 2003

SABIHA QAZI, PH.D
PRIMARY EXAMINER